

if a fairly reliable demonstration of the influence of fresh air alone had been made.

**SUMMARY.** Treatment of children in an open-air shed in winter increases their vitality and resistance to disease more powerfully than medicines.

Pneumonias run a short course and show a very low mortality. Certain abnormal conditions of the blood will rapidly improve with little or no medical treatment.

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### A PRELIMINARY REPORT ON PNEUMONIA IN CHILDREN, WITH SPECIAL REFERENCE TO ITS EPIDEMIOLOGY.<sup>1</sup>

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THE importance of pneumonia as a cause of death is hardly to be exaggerated. According to the United States census of 1900, pneumonia accounts for 3 per cent. of all diseases, with a mortality rate of 6.6 per cent., or of 12.7 per cent. if only medical cases are considered. It averages not less than 1.5 to 2.3 deaths per 1000 persons living. If pneumonia may be called the "old man's friend," it is just as certainly the enemy of youth, and especially of infancy. During early life the most common sort of organic disease is the lung, and some form of pneumonia is a large—perhaps the largest—factor at the present time in infant mortality. It is perhaps the only infectious disease in which the etiological cause supposedly is well understood whose incidence and rate have not been affected by such knowledge.

It is a matter of reproach to the profession that one hundred years of progress and varied methods of prevention and treatment have not affected the mortality rate of pneumonia in either adults or children.

The importance of pneumonia as a disease of infancy is well illustrated from the following mortality table of 1000 cases, which covers a period of the last nine years in the Babies' Wards of the New York Post-Graduate Hospital. The children were all under six years of age.

<sup>1</sup> Read at the Annual Meeting of the American Pediatric Society, May, 1915.

TABLE I.—1000 CASES OF PNEUMONIA FROM THE BABIES' WARDS OF THE NEW YORK POST-GRADUATE HOSPITAL.

		Per cent.
Cured . . . . .	513	51.3
Dead . . . . .	343	34.3
Improved . . . . .	62	6.2
Unimproved . . . . .	15	1.5
Termination not known . . . . .	4	0.4
Transferred . . . . .	63	6.3
Total . . . . .	1000	100.0

That this mortality rate is not excessive is shown by a death rate of 33.1 per cent. obtained from a series of 410 cases collected by Holt.<sup>2</sup> Holt's series included 223 cases of bronchopneumonia and 187 cases of lobar pneumonia in children. The age incident is apparently about the same in the two series. Pneumonias secondary to infectious diseases, such as whooping cough, measles, etc., are not included in either group of cases.

Pfaundler has made the observation that children are ill of nutritional disturbances, but that they die of infection. The truth of that statement is supported by 84 of our cases of pneumonia, which were frankly secondary to other disturbances, with a mortality rate of 52 per cent. Of these 84 cases, 24 occurred as a complication of malnutrition, rickets, and enteritis, with a death rate of 62.5 per cent.

From the clinical stand-point, pneumonia seems naturally to fall into two groups, namely, (1) bronchopneumonia, and (2) lobar pneumonia. The differentiation between the two types is important from the stand-point of prognosis, of treatment, and of prevention, and undoubtedly could and should be made more frequently. It is proposed tentatively to prove that the two conditions of bronchopneumonia and lobar pneumonia are not identical either pathologically or bacteriologically.

Bronchopneumonia undoubtedly occurs as a primary condition, but most frequently is secondary to other diseases, such as bronchitis or a moderate or severe intestinal disturbance. A large percentage of the cases in children occur during the first two years of life, though it may occasionally be met with at any age. Of 415 cases treated in the Babies' Wards of the Post-Graduate Hospital during the first three years of life, 41 per cent. died. In the following table it will be noted that the number of cases of bronchopneumonia rapidly diminishes after the second year, so that in this series of 1000 cases, of which 445 were bronchopneumonia, there are only 31 cases of bronchopneumonia between the ages of four and six years. In other words, of 445 cases of bronchopneumonia, 414 were infections of the first three years of life, and more than half of all the cases in this group occurred during the first year.

<sup>2</sup> Diseases of Infancy and Childhood, 6th ed., pp. 515-535.

TABLE II.

	Post-graduate cases.		Holt's cases.	
	Cases.	Mortality, per cent.	Cases.	Mortality, per cent.
During the 1st year . . . . .	236	52.2	202	66.0
" 2d year . . . . .	155	29.0	102	55.0
" 3d year . . . . .	33	24.2	33	33.0
" 4th year . . . . .	13	0.0	6	16.0
" 5th year . . . . .	13	0.0	3	0.0
" 6th year . . . . .	5	0.0		

Of the lobar pneumonia cases there were 227, and they are fairly evenly distributed throughout the first six years, though the first and second years include more than half the total number. It will be noted that the mortality rate is distinctly lower than for bronchopneumonia, being for the entire six years 28.1 per cent. If the first two years of high mortality are eliminated the death rate falls to 10.8 per cent.

In the following table is seen the incident of mortality by age in 227 cases of lobar pneumonia studied:

TABLE III.—LOBAR PNEUMONIA.

	Cases.	Mortality, per cent.
During 1st year . . . . .	75	40.2
" 2d year . . . . .	97	34.0
" 3d year . . . . .	31	12.9
" 4th year . . . . .	25	16.0
" 5th year . . . . .	21	0.0
" 6th year . . . . .	14	0.7

Judging from this series of 1000 cases of pneumonia, empyema is not a frequent complication. In all there were 41 cases, or 4.1 per cent., of empyema, of which 5 followed bronchopneumonia, the other occurring as a complication of lobar pneumonia.

Pathologically, it is questionable whether empyema ever occurs in a true case of bronchopneumonia. Wollstein and Meltzer,<sup>3</sup> in experimental bronchopneumonia on dogs, by means of intrabronchial insufflation, found practically complete absence of pleurisy in 20 experiments, while in true lobar pneumonia there was always a definite pleurisy even in non-fatal cases. Consequently, there must be some questioning of the 5 cases in this series which appear as a complication of bronchopneumonia. A few cases of empyema due to streptococcus have been reported, but the only case which has come directly under our observation was one of *Streptococcus hemolyticus*, occurring as a complication of an undoubted lobar pneumonia due to the pneumococcus.

It should be added that these 41 cases include only those empyemas which occurred as a complication of pneumonia treated in the wards, and consequently have no relation to the total number of empyemas admitted to the hospital.

<sup>3</sup> Jour. Exper. Med., 1912, xvi, 126.

In a study of groups of pneumonia by months it may be easily shown that the mortality rate at certain times is unusually high, as, for instance, during January and February of 1915. The large number of cases which were fatally ill during these months, which was much higher than for corresponding months of other years—in fact, was the inspiration for the special bacteriological study—the results of which are detailed in this paper.

The most obvious explanation for the variation of the mortality rate of pneumonia from year to year and from month to month is found in a difference in the virulence of the pneumococcus, a highly virulent organism resulting in many deaths and extraordinary severe pneumonias; an organism of low virulence, on the other hand, giving an infection in which recovery is the more common outcome.

Opposed to the argument that pneumonia arises when organisms of increased virulence reach the lung is the fact that pneumonia rarely occurs in epidemics. A few such epidemics, however, have been described, the most widely advertised of which occurred in Panama during the first year of the American occupation, and the one in South Africa, which reached such proportions as to seriously menace the working of the mines. Curschmann<sup>4</sup> describes an epidemic which was supposed to be due to influenza, in which cultures showed, in 49 cases, pneumococci in almost pure culture. The organisms were highly virulent for mice, and presented other characteristics of pneumococci. Leeds<sup>5</sup> describes another such epidemic in which a most careful search for the influenza bacillus was completely negative and the infecting organism was unquestionably the pneumococcus. A careful scrutiny of our cases fails to reveal any evidence of an epidemic or even of a house infection. In 50 cases very carefully studied from all stand-points there is only 1 case in which the pneumococcus was apparently transmitted from a twin sister, and in this instance the type was that of a bronchopneumonia.

Cole,<sup>6</sup> following the method of Lamar and Meltzer, of bronchial insufflation with broth cultures of various strains of pneumococci, has been able to prove that in rabbits, at least, the production of lobar pneumonia is somewhat dependent on the race of organisms used. A pneumococcus having a very slight virulence may end in a recovery of the animal without lung lesions, while if the organism is too virulent the animal quickly succumbs to a septicemia, and at necropsy shows only a congestion and edema of the lungs. Lamar and Meltzer<sup>7</sup> were the first to regularly produce a lobar pneumonia in animals, though Wadsworth,<sup>8</sup> eight years earlier, by

<sup>4</sup> Münch. med. Wchnschr., 1909, lvi, 377.

<sup>5</sup> Ztschr. f. Hyg. u. Infectiouskrankh., 1912, lxxi, 3.

<sup>6</sup> Arch. Int. Med., 1914, xiv, 8.

<sup>7</sup> Jour. Exper. Med., 1912, xv, 133.

<sup>8</sup> AMER. JOUR. MED. SCI., 1904, cxxvii, 851.

carefully balancing the general resistance of the animal with the virulence of the race of pneumococci employed, and by injecting the organism intratracheally, produced in a series of rabbits a diffuse exudative inflammation like the acute lobar pneumonia seen in man.

Wollstein and Meltzer by the use of other organisms, such as streptococcus and influenza bacillus, produced on all occasions a diffuse lesion which resembled closely that seen in bronchopneumonia.

An important factor in the production of pneumonia in animals is the number of organisms which are used. Even in susceptible animals a considerable number of virulent organisms is necessary to produce an infection. Gillespie<sup>9</sup> carried on some important experiments which have a bearing on this problem of why, when a considerable number of virulent organisms is injected, there is multiplication and infection, while if only a few organisms are injected they fail to multiply. It has long been recognized that in starting a culture of pneumococci in broth the number of organisms used depends upon the amount of culture media. For instance, an ordinary loopful of pneumococci might be sufficient to start a growth in 10 c.c. of bouillon, and result in failure if a liter of bouillon were used. Even on serum agar the growth is more rapid and profuse if a stab into the culture is made and the smear started from this point. If the culture is made in a solid media, one organism probably produces a colony. Gillespie was able to show that if the inoculation were made on filter paper kept constantly wet by bouillon, a growth would occur with an inoculation of as small a number of organisms as is required in agar and with a much smaller number than is required to inoculate the bouillon. The conclusion was drawn that for growth to occur the pneumococcus must change the medium immediately surrounding it, and that where diffusion is great the local changes cannot be kept sufficiently constant unless there is a considerable number of organisms in close proximity. This observation has an important bearing on the production of pneumonia. It is not considered that in order to produce pneumonia any such number of pneumococci must be introduced into the infantile being as was necessary to cause a pneumonia in the animals experimented upon by Lamar and Meltzer, but it does appear to be reasonable to suppose that if by any process a few of the terminal bronchioles are occluded, forming a small closed cavity, that pneumococci would be in a situation favorable for their multiplication. According to Cole,<sup>10</sup> extension of the process apparently takes place, in adults, at least, from one lobe to another through the bronchi, as the study of large sections through lobes with beginning involvement shows. It is common knowledge that

<sup>9</sup> Jour. Exper. Med., 1913, xviii, 584.

<sup>10</sup> Loc. cit.

pneumonia in children in a large number of instances follows after a few days of coryza, cough, and not infrequently a bronchitis. It may well be that conditions of this nature, extending along the bronchi, produce a favorable environment for the growth of pneumococci, which, as may be seen from the following table, are so frequently present in the upper respiratory tract of children.

TABLE IV.—PLATE CULTURES OF NON-PNEUMONIA CASES SHOWING  
TYPES OF ORGANISMS PRESENT.

	Age.	Pneumo- coccus.	Strepto- coccus (hemolytic).	Strepto- coccus viridans.	Staphylo- coccus.
Regulation of diet	4 mos.	....	++	.....	+
"	2 mos.	..	++	.....	+
"	14 wks.	+	.....	+	+
"	16 mos.	....	++	.....	++
"	7 wks.	..	.....	.....	++
"	"	..	..	.....	++
"	1 mos.	.....	..	.....	++
"	"	.....	+	+++	+
"	4 mos.	.....	.....	.....	++
"	10 wks.	.....	++	.....	++
"	4 mos.	..	.....	.....	++
"	5 wks.	..	++	.....	+
Malnutrition	3 mos.	..	.....	.....	+
Tertian malaria	12 mos.	.....	.....	.....	+
Hypertrophic tonsils and anemias	31 mos.	.....	+	.....	++
Acute intestinal toxemia	21 yrs.	.....	+	.....	+
Tuberculous peritonitis	24 mos.	+	+++	.....	+
Chronic endocarditis	5 yrs.	.....	+++	.....	+
Regulation of diet	12 mos.	.....	+++	.....	+
Empyema	31 yrs.	+	+++	+	+
Pneumonia	4 yrs.	++	.....	.....	+
Rickets	14 yrs.	.....	.....	.....	+
Otitis media and rickets	24 mos.	+	++	.....	+
Pyelonephritis	24 mos.	.....	.....	++	+
Hospitalism	4 mos.	++	.....	.....	+
Eczema	15 mos.	.....	++	.....	+
Von Jaksch pseudoleukemia	3 yrs.	+	+	++	+

The table shows the results of plate culture of sputum in blood agar. Where necessary the pneumococcus findings were verified by inoculation into mice, but, as a rule, the color of the colony, the morphology, and the action of bile upon the organism served to identify it. The specimen was nearly always taken from the upper part of the larynx with a bent applicator. In addition to this series, in which the lung, with one or two exceptions, was free of any known lesion, smears were made from 23 cases of lobar pneumonia in which the sputum was virulent for mice. In all of these a Gram-positive diplococcus was found, and in nearly every case it was the predominating organism, with a few scattered streptococci and staphylococci. In 10 cases of mild bronchopneumonia, the sputum of which did seem to be virulent for mice, the predominating organism was in 5 cases streptococcus; 2 cases each of staphylococcus and influenza bacillus; and in 1 case, tuberculosis bacilli with other organisms.

A few pneumococci were found in four of the series of bronchopneumonia studied, and it is possible that if a larger or more char-

acteristic specimen found could have been obtained that the sputum would have been found virulent for mice.

There were 8 cases of bronchopneumonia in which the sputum was virulent for mice, and in all of these a large number of pneumococci were found in the smears. There were, in addition, however, many other organisms, chiefly of the streptococcus and staphylococcus groups, so that these infections could be fairly labelled as mixed infections. These findings would explain in a measure the difference between a bronchopneumonia and a lobar pneumonia—the bronchopneumonia being a mixed infection, or an infection chiefly with a single type of organism other than the pneumococcus. For this reason the inflammation is peribronchial in character and consists primarily of an infiltration of interstitial tissue with leukocytes. The exudate into the alveoli is moderate and contains little or no fibrin. In lobar pneumonia the inflammation is due chiefly or entirely to the pneumococcus and is not peribronchial in character, and the framework of the lung is free of infiltration. The exudate is considerable and contains a large amount of fibrin. According to Wollstein and Meltzer, slightly virulent or non-virulent pneumococci produce an exudate that resembles that of a virulent streptococcus, in the small amount of fibrin present in the exudate.

The question naturally arises as to why infection occurs at all. It has just been shown that pneumococci were found by cultural methods in approximately 25 per cent. of the throats of small children examined in a routine manner in our wards (lungs free). There is no evidence to show that the organisms normally in the throat differ from those which cause pneumonia. There is considerable evidence that different races of pneumococci vary in their virulence toward animals. But the fact remains that some of these organisms which have little virulence for animals have been recovered from cases of severe pneumonia. Whether the resistance to pneumococci has temporarily been lowered in these patients sick with pneumonia is a speculative question to which no reply has apparently been made. It may be believed that the infection is the result of a combination of circumstances, such as the natural or acquired resistance of the individual, the state of the vitality of the individual, local changes in the respiratory tract which precede the infection, and, finally, the virulence of the organism.

Dochez and Gillespie,<sup>11</sup> in their important study, have been able to show that the pneumococcus is a family, which, by the extraordinarily specific methods developed from the study of immunity, can be subdivided into many races having varying degrees of virulence. They liken their subdivision of the family of pneumococcus to other grosser methods of classification, such as differ-

<sup>11</sup> Jour. Amer. Med. Assn., 1913, lxi, 723.

ences in growth or cultural characteristics that are sufficient in certain groups of organisms for differentiation. From the etiological stand-point they do not consider these fine lines of division as important, but from that of specific therapy these differences are of primary importance. At the Rockefeller Institute, under the direction of Dr. Cole, they began in 1910 to use an immune serum that was prepared by injecting a horse with a culture of pneumococcus obtained from Professor Neufeld, the same race he had used in the production of his immunized serum. The protective power of this serum for mice was found by Dochez<sup>12</sup> to be effective in only about one-half the cases. A biological classification of pneumococci was then undertaken by Dochez and Gillespie.<sup>13</sup> Rabbits were immunized to each race of pneumococci, and the protection afforded by these different rabbit serums against all other races of pneumococci was determined.

A considerable number were found to show cross-protection, that is, a serum prepared by injections of one of the number acted on all the races of this group. A horse was then immunized to one of this group and the serum was called Serum No. 2. In this way the pneumococci obtained from all cases of pneumonia were separated into four groups.

Group I contains all those races against which Serum No. 1 is effective.

Group II contains all those races against which Serum No. 2 is effective.

Group III consists of all the organisms of the so-called 'Pneumococcus mucosus' type. The individual organisms show a voluminous capsule containing medium-sized, closely approximated cocci with definitely round ends. They produce a sticky exudate in animals and on solid media a moist, transparent mass.

Group IV includes all the cases against which Serum No. 1 and Serum No. 2 are not effective and which from their other properties do not belong in Group III. This group seems to consist of entirely isolated individuals, the significance of which it is difficult to interpret according to Dochez. It may be that this heterogeneous group may be representative of the type of pneumococcus found in the normal mouth.

In our experiments there were obtained eleven strains of pneumococci from the throats of children having no lung involvement all of which belonged in Group IV. In one case pneumococci of Group I were obtained before physical examination revealed a lobar pneumonia.

The chief difficulty met with in babies and small children was the obtaining of a sufficient specimen for a direct mouse injection. The method which was finally adopted was a simple one, con-

<sup>12</sup> Jour. Exper. Med., 1912, xvi, 680.

<sup>13</sup> Jour. Amer. Med. Assn., 1913, lxi, 727.

sisting of a tongue depressor, placed well back on the tongue and down in the throat. This method resulted in some gagging and more or less coughing, which in most cases brought a plug of mucus up into the throat, which was caught on the spatula. While the amount obtained was often scanty, only occasionally was it necessary to take a second or a third specimen. The method used from this point closely follows Dr. Cole's description of the method used at the Rockefeller Institute. The sputum was immediately injected into the peritoneal cavity of the mouse. The peritoneal cavity was washed with salt solution as soon as the mouse showed symptoms of being severely ill. The cells were thrown down in a centrifuge, a suspension of the organisms being thus obtained. The agglutination test was at once made with Serum No. 1 and Serum No. 2.

At the same time that this was being done a very small amount of blood was withdrawn from the heart and smeared across a blood-agar plate. In twenty-four hours the type of colony can be studied on the plates and further agglutination or cultural tests made. The work was checked by a Gram and a capsule stain (His's method) and by lysis of the bacteria with bile. In making the agglutination tests from the peritoneal washings the amount used depended somewhat upon the opacity of the solution containing the suspension, and 0.3 c.c. of the serum was the amount employed.

Our final test was always made with an eighteen-hour-old broth culture inoculated from typical plate colonies. Equal amounts of the broth and serum were employed in the test (as a rule, 0.3 c.c. broth culture and 0.3 c.c. of serum). It was noted that a fairly high dilution of the serum often made it difficult to obtain an agglutination; but, as a matter of fact, the organisms seem to have the property of remaining suspended in the serum used, even though the serum was not diluted at all. Readings were made macroscopically at the end of one and two hours at 37° C., and again after standing twenty-four hours in the ice-box. Usually, agglutination was visible in fifteen minutes or half an hour, and consisted at first of a fine granulation followed by a sinking of clumps which form a thin layer on the bottom of the tube that could not be broken up even by vigorous shaking.

The serum for Groups I and II was obtained through the kindness of Dr. Cole, at the Rockefeller Institute. Somewhat to our surprise, for we expected many of our pneumonias to fall into Group IV, our cases paralleled quite closely those at the Rockefeller Institute so far as groups are concerned. We obtained many more in Group II than Dr. Cole's published results would seem to warrant; but in a personal communication, Dochez has told us that he too had an unusually large number of organisms fall into Group II during the past winter. The following table briefly summarizes our results:

	Cases of lobar pneu- monia.	Cases of broncho- pneu- monia.	Pri- mary.	Second- ary.	Deaths.	Cures.	Total number of cases.	Percentage in each group (cases with no results not included).	Per cent. of mor- tality.
Group I	9	2	9	12	1	10	11	22.9	9
Group II	11	3	12	12	5	9	14	29.3	36
Group III	1	3	2	12	1	3	4	8.3	25
Group IV	7	12	6	11	4	15	19	39.8	21
No result	3 <sup>a</sup>	12	..	..	..	..	23 <sup>a</sup>		
Total	..	..	..	..	..	..	71		

It will be noted that there are 48 cases in which it has been possible to determine the group to which the pneumococcus causing the infection belongs. Of the 23 cases in which it was not possible, for one reason or another, to obtain a pneumococcus culture, in at least 3 a positive result would in all probability have been obtained with a proper specimen. Empyema occurred as a complication in 7 of these cases. With one exception, the organism recovered from the empyemas was the pneumococcus, of which 2 belonged in Group I, 3 in Group II, and 1 in Group IV. The seventh case gave a pure culture of *Streptococcus hemolyticus*.

Our mortality-rate for the groups, with the exception of Group IV, is somewhat lower than in the series published by Cole.<sup>16</sup> For purposes of comparison, mortality percentages for the two series are placed side by side.

	Our series.	Cole's series.
Group I . . . . .	9 per cent.	24 per cent.
Group II . . . . .	36 "	61 "
Group III . . . . .	25 "	60 "
Group IV . . . . .	21 "	7 "

The number of cases in both series is as yet insufficient for the determination of the absolute mortality rate in each group. As our series is based on children under six years of age, a comparison with Cole's adult cases is obviously unfair. Lobar pneumonia decidedly predominated in Groups I and II, while rather more than half the cases in our Group IV were clinically bronchopneumonia, while the cases dealt with by Dr. Cole are exclusively of the lobar type. Moreover, there is an actual difference in the mortality-rate in the two series, ours being 23 per cent., as opposed to Dr. Cole's 38 per cent. In all probability this marks another difference in the two series, as we used every pneumonia case that came into our children's service, while probably only very ill patients were sent to Dr. Cole's service at the Rockefeller Institute.

**SUMMARY.** From a study of a thousand cases we have established a mortality-rate for pneumonia of 34.3 per cent. It is admitted that this is probably a higher rate than obtains in private practice

<sup>a</sup> Two cases sputum taken after all symptoms had disappeared.

<sup>b</sup> Eight of these were control cases, having no lung involvement.

<sup>c</sup> Loc. cit.